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Research article

Demographics and prognosis of patients with pyogenic liver abscess due to *Klebsiella pneumonia* or other species

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ABSTRACT

Background: Pyogenic liver abscess (PLA) is a potentially life-threatening intra-abdominal infection. We compared the clinical features, treatments, and prognoses of patients who had *Klebsiella pneumonia* pyogenic liver abscess (KPPLA) and non-*Klebsiella pneumonia* pyogenic liver abscess (non-KPPLA).

Methods: A retrospective analysis was used to compare the medical records of KPPLA and non-KPPLA patients with positive pus cultures at a single hospital in China from January 2017 to December 2019.

Results: We examined 279 patients with definitively established PLA, 207 (74.2 %) with KPPLA, and 72 with non-KPPLA. The non-KPPLA group had a higher Charlson comorbidity index, longer hospital stay, longer duration of fever, and greater hospital costs. Multivariate analysis showed that alcohol intake (OR: 2.44, $P = 0.048$), cancer (OR: 4.80, $P = 0.001$), ICU admission (OR: 10.61, $P = 0.026$), resolution of fever OR: 1.04, $P = 0.020$), and a positive blood culture (OR: 2.87, $P = 0.029$) were independent predictors of primary treatment failure. Percutaneous needle aspiration (PNA) and pigtail catheter drainage (PCD) provided satisfactory outcomes, but PNA led to shorter hospital stays and reduced costs, especially in KPPLA patients whose abscesses were smaller than 10 cm.

Conclusion: KPPLA and non-KPPLA patients had some differences in comorbidities and treatment strategies, and non-KPPLA patients had a significantly worse prognosis.

1. Introduction

Infection is the most common cause of a pyogenic liver abscess (PLA), and this potentially life-threatening intra-abdominal condition has a high mortality rate and its incidence has increased worldwide during the last two decades [1]. A pathogenic examination is important for the diagnosis and successful treatment of these patients [2]. It is generally believed that *Escherichia coli* and *Streptococcus*

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are responsible for most cases of PLA in Western countries [3]. However, the prevalence of PLA from *Klebsiella pneumoniae* (KP) infection has increased significantly in China and Southeast Asia during recent years, and several studies reported that KP accounted for more than half of the positive culture results in Asian patients with PLA [4–6]. It is now believed that this significantly higher proportion of cases with KP pyogenic liver abscess (KPPLA) is related to improvements in pathogenic testing, increased susceptibility to KP infection, and the increased incidence of diabetes mellitus [7].

The use of effective antibiotic therapies, improvements in diagnostic imaging, and adoption of less invasive interventions, especially the widespread application of percutaneous needle aspiration (PNA) and pigtail catheter drainage (PCD), have reduced the mortality rate of patients with PLA, and it is now only about 6–14 % [1,8]. However, liver abscesses caused by KP infections are prone to invasive liver abscess syndrome, and infections by hypervirulent KP (hvKP) and the emergence of drug-resistant KP have dramatically increased the hospitalization costs and mortality of patients with PLA [7,9]. Some studies showed that PLA caused by other pathogens is relatively uncommon in China, although there have been no direct and extensive comparisons between the KPPLA and non-*Klebsiella pneumoniae* pyogenic liver abscess (non-KPPLA) in the Chinese population [4,10,11].

To further understand the differences in clinical characteristics, treatment efficacy, and prognosis of patients with PLA caused by different pathogens, we compared the general and clinical characteristics, underlying diseases, imaging features, laboratory indices, pathogenic features, treatments, and prognosis of KPPLA and non-KPPLA patients in our center. Our general purpose was to identify the best treatment options for different pathogens and to provide clinicians with an improved basis for treatment of PLA.

2. Methods

2.1. Study population

This retrospective study was conducted at the First Affiliated Hospital, Zhejiang University School of Medicine in Hangzhou (China). PLA was defined by the presence of the combination of specific clinical symptoms, microbiological characteristics, and imaging findings, based on established criteria [3]. All cases with confirmed diagnoses of liver abscess and positive pus cultures were enrolled from January 2017 to December 2019. Patients were excluded if they had negative pus cultures or abscesses caused by parasites or fungi. Patient outcome was classified as clinical cure (complete resolution of clinical symptoms plus significant radiological improvement at 4 weeks after the end of treatment) or as primary treatment failure [3]. This study was approved by the Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine (No. 2023-0115).

2.2. Clinical and microbiological data

All medical records were reviewed by analysis of the hospital database, which included clinical and radiological data, underlying diseases, microbiological findings from blood and pus cultures, treatments, and outcomes. Alcohol intake was defined as regular drinking of more than 20 g ethanol/day for women and more than 30 g ethanol/day for men, as previously described [12]. For culture preparation, pus from the liver was added to blood agar plates. Then, one plate was incubated aerobically and a second plate was incubated anaerobically at 37 °C for five days. Matrix-assisted laser desorption-ionization/time-of-flight mass spectrometry (MALDI-TOF MS, Bruker, France) was then used for pathogen identification. According to the recommendations of the Clinical Laboratory Standard Institute (CLSI), antimicrobial susceptibility testing was performed using the VITEK 2 system (BioMerieux, France) for all identified bacterial isolates [13].

2.3. Percutaneous needle aspiration

Pus from each cavity was evacuated using a disposable 18-gauge trocar needle. The abscess cavity was evaluated every 3 days using ultrasound, and aspiration was repeated if there was no significant decrease in the amount of pus. If there was no significant improvement after three aspirations, PCD or surgery was performed; these patients were not included in PCD group.

2.4. Percutaneous catheter drainage

Under ultrasound guidance, an 8 Fr pigtail catheter was placed into the cavity. Confirmation of entry was achieved by aspirating pus and maintaining continuous drainage. The daily accumulation of pus in the catheter was measured, and the catheter was intermittently rinsed with saline to prevent blockage. Ultrasound was performed every 3 days to assess the size and residual contents of the abscess. If clinical signs and ultrasound findings indicated improvement, the catheter was removed; treatment was regarded as a failure if the PCD was ineffective and surgery was required.

2.5. Statistical analysis

Descriptive analyses were conducted, and results were expressed as numbers (percentages) for categorical variables and as means ± standard deviations (SDs) or medians and interquartile ranges (IQRs) for continuous variables. To compare the KPPLA and non-KPPLA groups, Student's *t*-test was used for continuous variables and the Chi-square test was used for categorical variables. A multivariate logistic regression model was also used to identify the risk factors for primary treatment failure. This prognostic model had the following form: (regression coefficient B1) × (variable 1) + (regression coefficient B2) × (variable 2) + (regression coefficient

B3) × (variable 3) + …. SPSS version 22.0 (USA) was used to perform all statistical analyses.

3. Results

3.1. Patient characteristics

We retrospectively identified 279 patients at our institution who had PLA with definite etiology from January 2017 to December 2019. There were 207 patients (74.2 %) with KPPLA and 72 patients (25.8 %) non-KPPLA (Fig. 1, Table 1). These two groups were similar in mean age (KPPLA group: 57.2 ± 14.0 years, non-KPPLA group: 57.1 ± 14.0 years) and gender distribution. The non-KPPLA group had greater prevalences of admission to a surgical ward, history of surgery, and multiple underlying diseases (cancer, cholelithiasis, HBV infection, and liver cirrhosis), and also had a higher Charlson comorbidity index (all $P < 0.05$). A total of 50 patients had tumors, and this included 16 patients in the KPPLA group (4 with hepatocellular carcinoma, 4 with pancreatic cancer, 3 with cholangiocarcinoma, 3 with thyroid cancer, and 2 with colorectal cancer) and 34 patients in the non-KPPLA group (16 with hepatocellular carcinoma, 5 with pancreatic cancer, 5 with cholangiocarcinoma, 4 with colorectal cancer, 3 with gastric cancer, and 1 with gallbladder cancer). The KPPLA group had greater prevalences of diabetes mellitus and fatty liver (both $P < 0.05$), and also had 12 patients with invasive liver abscess syndrome, 4 with lung abscesses, 4 with endophthalmitis, 2 with necrotizing fasciitis, 2 with prostatic abscesses, and 1 with a brain abscess.

Fever was the most common symptom in both groups (KPPLA group: 98.6 %, non-KPPLA group: 97.2 %, $P = 0.466$), and the two groups also had no significant differences in leukocyte count, serum albumin, aspartate transaminase (AST), and serum creatinine (SCr). The KPPLA group had higher levels of alanine transaminase (ALT) and C-reactive protein (CRP), but lower levels of alkaline phosphatase (ALP) and bilirubin (all $P < 0.05$). The duration of hospitalization, duration of fever, prognosis, and hospitalization costs were lower in the KPPLA group (all $P < 0.05$).

3.2. Characteristics of liver abscesses and pathogens

We analyzed the imaging results in all 279 patients (Table 2). The average of abscess diameter was 7.3 ± 2.6 cm, and 179 patients (64.2 %) had abscesses that were 5–10 cm. There were 190 patients (68.1 %) with abscesses in the right liver, 60 (21.5 %) with abscesses in the left liver, and 29 (10.4 %) with abscesses in the right and left liver. A total of 142 patients (50.9 %) had a single abscess, and 137 patients (49.1 %) had multiple abscesses. The KPPLA and non-KPPLA groups had no differences in the size, scope, or distribution of abscesses. However, more KPPLA patients received PNA and more non-KPPLA patients received PCD ($P < 0.05$).

The blood cultures were positive in 40 of 279 patients (KPPLA group: 26, non-KPPLA group: 14), and all of these results were consistent with the pus culture results. Antibiotic sensitivity testing in the KPPLA group (Fig. 2A) indicated the pathogens in 73 patients (35.3 %) were susceptible to all tested antibiotics. In addition, 94 isolates (45 %) were resistant to ampicillin, 39 (18.8 %) were resistant to macrodantin, 21 (10.1 %) were resistant to cefuroxime, 14 (6.8 %) were resistant to ceftazidime, 14 (6.8 %) were resistant to piperacillin-tazobactam, 13 (6.3 %) were resistant to meropenem, and 3 (1.4 %) were positive for ESBL. Species identification in the non-KPPLA group (Fig. 2B) indicated 14 patients (19.4 %) with *Escherichia coli*, 12 patients (16.7 %) with pathogens in the

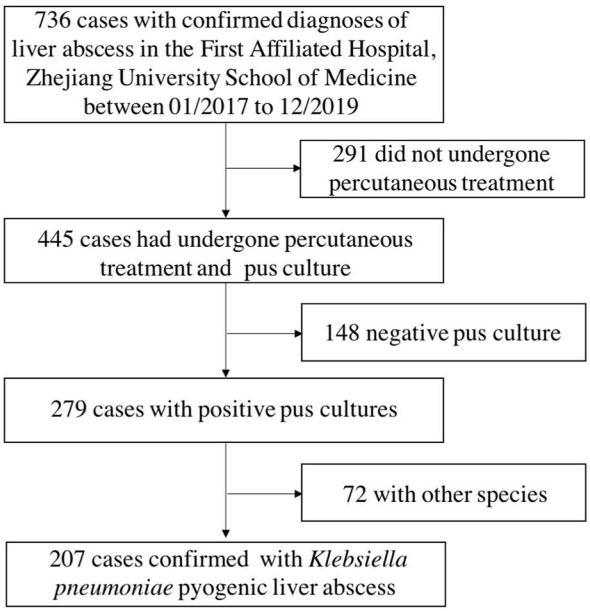

Fig. 1. Flow diagram of the procedures used to identify cases with confirmed diagnoses of liver abscess and positive pus cultures.

Table 1
Comparison of clinical characteristics in patients with pyogenic liver abscess.

Patients characteristics	Total (n = 279)	KP (n = 207)	Non-KP (n = 72)	P value
Age	57.2 ± 14.0	57.1 ± 14.0	57.3 ± 14.3	0.923
Male gender	192 (68.8)	144 (69.6)	48 (66.7)	0.649
Area (Urban)	127 (45.5)	97 (46.9)	30 (41.7)	0.448
Surgical ward	47 (16.9)	23 (11.1)	24 (33.3)	0.000
Married	259 (92.8)	192 (92.8)	67 (73.1)	0.536
Smoke	92 (33.0)	67 (32.4)	25 (34.7)	0.715
Alcohol intake	95 (34.1)	71 (34.3)	24 (33.3)	0.882
Disease				
Diabetes mellitus	111 (39.8)	102 (49.3)	9 (12.5)	0.000
Cholelithiasis	48 (17.2)	26 (12.6)	22 (30.6)	0.000
Cancer	50 (17.9)	16 (7.7)	34 (47.2)	0.000
HbsAg	24 (8.6)	12 (5.8)	12 (16.7)	0.004
Liver cirrhosis	21 (7.5)	9 (4.3)	12 (16.7)	0.001
Fatty liver	26 (9.3)	25 (12.1)	1 (1.4)	0.007
Hypertension	79 (28.3)	65 (31.4)	14 (19.4)	0.053
Charlson comorbidity index score	0.9 ± 1.0	0.7 ± 0.8	1.4 ± 1.4	0.000
Previous surgery	35 (12.5)	15 (7.2)	20 (27.8)	0.000
Fever	274 (98.2)	204 (98.6)	70 (97.2)	0.466
Leukocyte (10^9/L)	10.5 (8.2–13.9)	10.9 (8.5–14.5)	9.8 (6.9–13.2)	0.115
C-reactive protein (mg/L)	120.8(71.3–178.6)	126(75.5–184.4)	109.8(52.3–164.0)	0.019
Albumin(g/dL)	31.1 (27.0–34.9)	31.2 (27.4–35.1)	30.3 (26.5–34.1)	0.127
Alanine transaminase (u/L)	40 (23–72)	45 (25–79)	28.5 (20–44)	0.013
Aspartate transaminase (u/L)	29 (21–50)	28 (20–47)	29.50 (22–56)	0.284
Alkaline phosphatase (u/L)	147 (103–202)	139 (97–186)	177 (117–273)	0.000
Bilirubin mg/dl	13.0 (8.4–21.9)	12.4 (8.0–20.2)	15.0 (9.0–30.9)	0.000
Serum creatinine (μmol/L)	63 (51–75)	65 (52–75)	58 (46–77)	0.064
No. of patients requiring subsequent surgery	3 (1.1)	1 (0.5)	2 (2.8)	0.105
Positive blood culture	40 (14.3)	26 (12.6)	14 (19.4)	0.152
fever duration	6(2–12)	6 (3–11)	8 (3–17)	0.003
ICU admission	6 (2.2)	4 (1.9)	2 (2.8)	0.671
Death	8 (2.9)	2 (1.0)	6 (8.3)	0.001
No. of treatment failure	29 (10.4)	13 (6.3)	16 (22.2)	0.000
Hospital stay	14 (9–20)	13 (9–19)	15 (9–24)	0.010
Hospitalization costs (yuan)	24529.6 (16995.6–39458.8)	23236.6(16013.8–33774.7)	35035.4 (20962.5–53406.8)	0.000

Abbreviations: KP, *Klebsiella pneumonia*.

Table 2
Image characteristics of 279 patients with pyogenic liver abscess.

Characteristics	Total (n = 279)	KP (n = 207)	Non-KP (n = 72)	P vaule
Number				0.712
Single	142 (50.9)	104 (50.2)	38 (52.8)	
Multiple	137 (49.1)	103 (49.8)	34 (47.2)	
Site				0.806
Right	190 (68.1)	143 (69.1)	47 (65.3)	
Left	60 (21.5)	44 (21.3)	16 (22.2)	
Both	29 (10.4)	20 (9.7)	9 (12.5)	
Size				0.414
<5 cm	55 (19.7)	39 (18.8)	16 (22.2)	
5 ≤ diameter <10 cm	179 (64.2)	140 (67.6)	39 (54.2)	
≥10 cm	45 (16.1)	28 (13.5)	17 (23.6)	
Mean diameter (cm)	7.3 ± 2.6	7.3 ± 2.5	7.5 ± 3.0	0.601
Treatment				0.025
PNA	96 (34.4)	79 (38.2)	17 (23.6)	
PCD	183 (65.6)	128 (61.8)	55 (76.4)	

Abbreviations: KP, *Klebsiella pneumonia*; PNA, percutaneous needle aspiration; PCD, percutaneous catheter drainage.

Streptococcus anginosus group, 10 patients (13.9 %) with *Staphylococcus* sp., 7 patients (9.7 %) with *Enterococcus faecium*, 5 patients (6.9 %) with *Enterococcus faecalis*, and 24 patients (23.7 %) with other pathogens.

3.3. Treatment and outcome following PNA and PCD

Patients received intravenous third generation cephalosporins, and the antibiotic therapy was adjusted according to the results of drug sensitivity testing. In addition, 183 patients (55.6 %) received PCD and 96 (34.4 %) received PNA (Table 3). PCD was the most frequent method of pus removal in the KPPLA group (128/207, 61.8 %) and the non-KPPLA group (55/72, 76.4 %). Among all 279

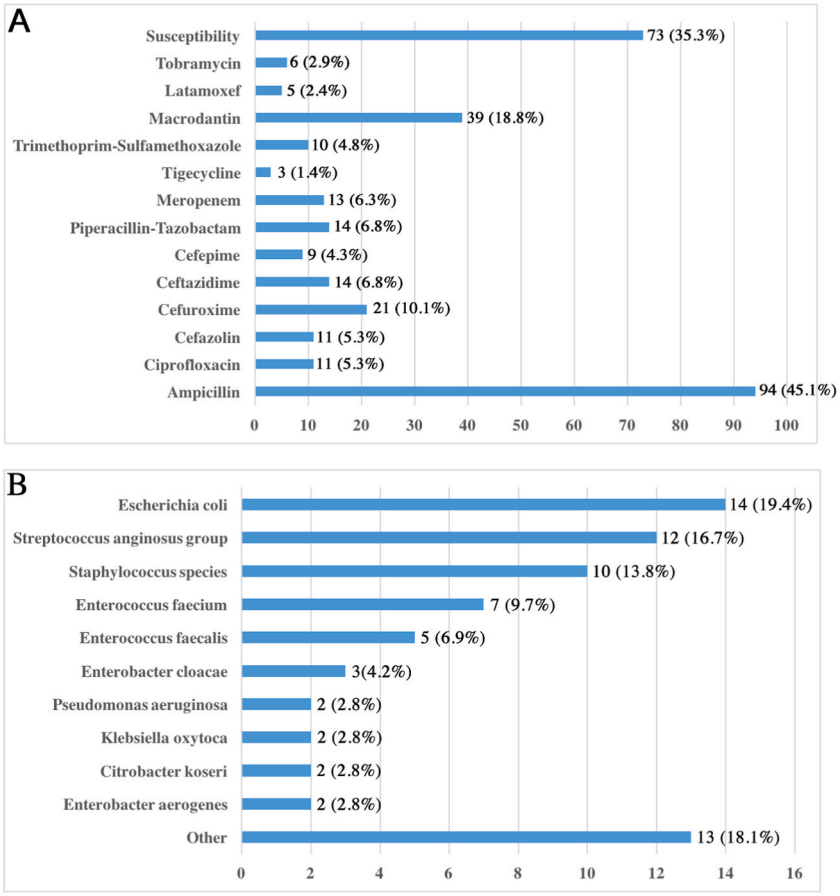

Fig. 2. Sensitivity of *Klebsiella pneumoniae* isolates to different antibiotics in the KPPLA group (A). Bacterial species identified in the liver abscesses in the non-KPPLA group (B). Other pathogens include *Enterococcus avium*, *Enterobacter asburiae*, *Clostridium perfringens*, *Acinetobacter baumanii*, *Propionibacterium acnes*, *Actinomyces odontolyticus*, *Actinomyces naeslundii*, *Gemella mobillorum*, *Pseudomonas mendocina*, *Morganella morganii*, *Proteus vulgaris*, *Enterococcus casselifavus* and *Stenotrophomonas maltophilia*, each with one strain.

patients, PNA and PCD provided high efficacy and safety, with success rates of 93.8 % and 87.4 %, respectively. However, PNA led to fewer complications, shorter hospital stays, and lower costs (all $P < 0.05$). In the KPPLA group, PNA led to more rapid control of body temperature, shorter length of hospital stay, and reduced hospitalization costs (all $P < 0.05$). There were no statistically significant differences between the use of PNA and PCD in the non-KPPLA group.

Further analysis of the KPPLA group showed that PNA led to reduced length of hospital stay, reduced hospital costs, and more patients with reduced fever when the abscess diameter was less than 10 cm (Table 4). However, these two methods did not provide significantly different outcomes for patients with lesions larger than 10 cm.

3.4. Risk factors for primary treatment failure

Twenty-nine patients (10.4 %) experienced primary treatment failure, 13 in the KPPLA group (6.28 %) and 16 in the non-KPPLA group (22.2 %). Among these 29 patients, 8 (2.9 %) died and 21(7.5 %) received further treatment during the study period. The results of a multivariate analysis showed that alcohol intake (OR: 2.44, 95%CI: 1.01, 5.94, $P = 0.048$), cancer (OR: 4.80, 95%CI 1.96, 11.78, $P = 0.001$), ICU admission (OR: 10.61, 95%CI 1.32, 85.33, $P = 0.026$), resolution of fever (OR: 1.04, 95%CI 1.01, 1.07, $P = 0.020$), and positive blood culture (OR: 2.87, 95%CI: 1.01, 1.07, $P = 0.029$) were independent risk factors for primary treatment failure (Table 5). Receiver operating characteristic (ROC) analysis, which was based on the results of the multivariate analysis, showed that the modified model had an area under the curve (AUC) of 0.782, an optimal cut-off point (Youden's index) at 0.57, a sensitivity of 69.0 %, and a specificity of 88.0 % (Fig. 3). The final prognostic model was: (0.894 × alcohol intake) + (1.569 × cancer) + (2.361 × ICU admission) + (1.054 × positive blood culture) + (0.039 × resolution of fever).

4. Discussion

We identified 279 patients at our institution in Hangzhou who had PLA with definitive pathogen identification between January

Table 3
Outcome comparison of PNA and PCD between KPPLA and non-KPPLA.

Patients characteristics	Total (n = 279)			KPPLA (n = 207)			Non-KPPLA (n = 72)		
	PNA (n = 96)	PCD (n = 183)	P value	PNA (n = 79)	PCD (n = 128)	P value	PNA (n = 17)	PCD (n = 55)	P value
No. of procedure related complications	38 (39.6)	99 (54.1)	0.021	32 (40.5)	69 (53.9)	0.061	6 (35.3)	30 (54.6)	0.170
Resolution of fever	5 (2–8)	7 (3–13)	0.064	4 (2–7)	7 (4–12)	0.016	9 (5–24)	7 (2–15)	0.537
Hospital stay	12 (8–15)	14 (10–21)	0.010	12 (8–15)	14 (10–20)	0.005	14 (9–25)	15 (9–24)	0.901
No. of patients requiring subsequent surgery	2 (2.1)	1 (0.6)	0.239	1 (1.3)	0 (0)	0.204	1 (5.9)	1 (1.8)	0.380
No. of patient death	3 (3.1)	5 (2.7)	0.853	0 (0)	2 (1.6)	0.266	3 (17.7)	3 (5.5)	0.115
Treatment failure	6 (6.3)	23 (12.6)	0.101	2 (2.5)	11 (8.6)	0.081	4 (23.5)	12 (21.8)	0.884
Hospitalization expenses	18722.8 (13275.0–29532.0)	28823.6 (19475.9–44277.3)	0.028	16995.6 (12557.9–24925.6)	26218.8 (19273.5–37901.8)	0.011	30663.5 (21061.4–50038.1)	35529.9 (20266.5–54056.6)	0.753

Abbreviations: PNA, percutaneous needle aspiration; PCD, percutaneous catheter drainage; KPPLA, *Klebsiella pneumonia* pyogenic liver abscesses.

Table 4
Outcome comparison between PNA and PCD in different sizes of KPPLA (n = 207).

Patients characteristics	diameter < 5 cm (n = 39)			5 ≤ diameter <10 cm (n = 140)			diameter ≥10 cm (n = 28)		
	PNA (n = 22)	PCD (n = 17)	P value	PNA (n = 49)	PCD (n = 91)	P value	PNA (n = 8)	PCD (n = 20)	P value
No. of procedure-related complications	8 (36.4)	9 (52.9)	0.061	21 (42.9)	48 (52.8)	0.267	3 (37.5)	12 (60.0)	0.298
Resolution of fever	3 (1–7)	5 (2–14)	0.016	4 (2–7)	7 (4–12)	0.012	7 (5–8)	10 (5–12)	0.381
Hospital stay	12 (8–16)	14 (9–18)	0.005	10 (7–14)	14 (10–20)	0.000	12 (13–18)	17 (12–21)	0.565
No. of patients requiring subsequent surgery	0 (0)	0 (0)	NA	1 (2.0)	0 (0)	0.174	0 (0)	0 (0)	NA
No. of patient death	0 (0)	1 (5.9)	0.266	0 (0)	1 (1.1)	0.465	0 (0)	0 (0)	NA
No. of treatment failure	0 (0)	2 (11.8)	0.081	2 (4.1)	8 (8.8)	0.305	0 (0)	1 (5.0)	NA
Hospitalization expenses	16155.7 (10636.3–32005.9)	23945.5 (16078.3–33046.9)	0.011	16721.2 (12933.9–22750.0)	26576.7 (19292.6–37220.0)	0.001	25166.8 (17580.0–299886.2)	29450.7 (22006.4–41924.8)	0.356

Abbreviations: PNA, percutaneous needle aspiration; PCD, percutaneous catheter drainage; KPPLA, *Klebsiella pneumonia* pyogenic liver abscesses.

Table 5
Risk factors related to primary treatment failure for 279 patients with PLA according to the univariate and multivariate analyses.

Variables	Success (n = 250)	Failure (n = 29)	Univariate analysis		Multivariate analysis		
			OR (95 % CI)	P value	B value	OR (95 % CI)	P value
Alcohol intake	79 (31.6)	16 (55.2)	2.66 (1.22–5.81)	0.014	0.894	2.44 (1.01–5.94)	0.048
Cancer	37(14.8)	13 (44.8)	4.67 (2.08–10.52)	<0.001	1.569	4.80 (1.96–11.78)	0.001
Non-Kp infecton	56 (22.5)	16 (55.3)	4.17 (1.89–9.18)	<0.001			
Liver cirrhosis	16 (6.4)	5 (17.2)	3.05 (1.03–9.05)	0.045			
Previous surgery	27 (10.8)	8 (27.6)	3.15 (1.27–7.79)	0.013			
Alkaline phosphatase (u/L)	142 (99–193)	200 (119–270)	1.003 (1.001–1.005)	0.012			
ICU admission	2 (0.8)	4 (13.79)	19.84 (3.46–113.77)	0.001	2.361	10.61 (1.32–85.33)	0.026
Positive blood culture	29 (11.6)	11 (37.93)	4.66 (2.00–10.83)	<0.001	1.054	2.87 (1.11–7.40)	0.029
Resolution of fever, days	6 (2–11)	10 (6–19)	1.05 (1.02–1.08)	0.002	0.039	1.04 (1.01–1.07)	0.020
Hospital stay	13 (9–20)	15 (11–28)	1.04 (1.01–1.07)	0.002			

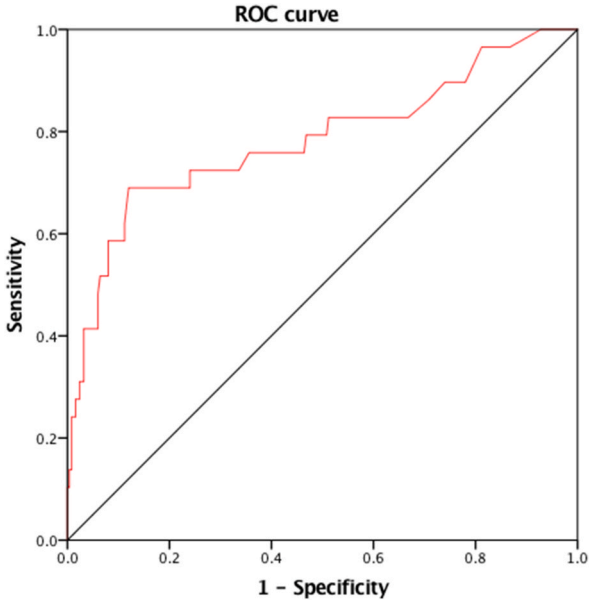

Fig. 3. Receiver-operating characteristic curve derived from the multivariate prognostic model for primary treatment failure in patients with PLA.

2017 and December 2019, and then compared the characteristics of patients with KPPLA and non-KPPLA. Our two major results were that KP infection was the major causative pathogen and that patients with non-KPPLA infections had worse outcomes in terms of primary treatment failure and mortality.

The prevalence of KPPLA has increased significantly worldwide [14,15], and KP was previously reported as the most common pathogen in Chinese patients with PLA [4,6], consistent with our results. However, we found a lower overall mortality rate (2.9 %) than reported by Yu et al. (7.8 %, 5/64) [1], and in other previous studies [8]. There is evidence that several risk factors have strong correlations with poor prognosis in PLA patients, including age, underlying diseases, and delayed treatment [16,17]. Identification of the characteristics of PLA patients who are more susceptible to infection by KP or non-KP species may help clinicians to make better treatment decisions in a timely manner. We found that many PLA patients had diabetes, hypertension, cancer, and cholelithiasis as comorbidities. Several other studies of PLA suggested that the incidence of KP infection was associated with underlying diabetes mellitus [18–20]. In agreement, we found that nearly half of the patients in our KPPLA group had diabetes, a much higher percentage than in our non-KPPLA group (12.5 %, $P < 0.05$). Diabetes can also increase the susceptibility to invasive liver abscess syndrome [21]. This may be because poor control of glucose levels leads to impaired neutrophil activity and phagocytosis, thereby reducing bacterial clearance and the efficient control of infections [5,22]. Biliary tract infection is one of main pathogenic mechanisms responsible for PLA, and is more common in non-KP infections, such as those from *Enterococcus* [23]. Cholelithiasis and neoplastic obstruction are common causes of biliary tract disease, and we found significantly higher proportions of patients with these two conditions in our non-KPPLA group.

Antibiotic therapy plays a crucial role in the treatment of PLA, and early identification of the causative pathogen by pus culture or blood culture, followed by drug sensitivity testing, provides important information for selection of the most appropriate antibiotics [24]. After a diagnosis of KPPLA, the commonly used cephalosporin antibiotics or β-lactamase inhibitor combinations can often achieve good efficacy. There are also some carbapenem-resistant KP, and although the percentage is not very high this must be

considered in clinical settings. The recent emergence of hvKP, which was first reported in Asia, is characterized by the hypermucoviscous phenotype in capsular serotypes K1 or K2. Infections by hvKP can lead to invasive and metastatic complications, and immunocompetent patients can also experience hvKP infections [25]. A study of PLA patients in China found that the hypermucoviscous phenotype accounted for 90 of 101 (89.1 %) KP isolates in these patients [26]. Although we did not perform testing for hvKP, antimicrobial resistance in hvKP is an emerging problem [25]. KPPLA is currently associated with a fairly low mortality rate, but this may change if there is an increasing prevalence of multidrug-resistant and hypervirulent strains.

In addition to antibiotic treatment, percutaneous intervention is also an important intervention for patients with PLA, because rapid removal of pus can significantly shorten the hospital stay, improve patient prognosis, and reduce hospitalization costs [1]. Over the past two decades, PNA and PCD have played increasingly important roles in treating liver abscesses, although there is still considerable debate as to which is superior [27,28]. Our KPPLA and non-KPPLA groups both had higher prevalences of infections in the right liver, possibly because of the larger size of the right hepatic lobe and because this lobe receives a greater portal blood supply. Our KPPLA and non-KPPLA groups were also similar in terms of abscess size, abscess location, and number of abscesses. Our overall treatment success rate (from PNA or PCD) was 89.61 %, and was unrelated to the causative pathogen. Some recent studies suggested were some differences in the efficacy of PCD and PNA depending on abscess size and pathogen species [1,27,28]. We also compared the effects of different modalities of pus removal in the KPPLA and non-KPPLA groups; there was no difference for the non-KPPLA group, but PNA was superior to PCD in the KPPLA group in terms of hospital stay and hospital costs, although both modalities provided good safety and efficacy. A subgroup analysis of the KPPLA group showed that PNA was significantly better than PCD in terms of hospital stay and hospitalization costs for patients with lesions less than 10 cm. Compared with PCD, PNA is easier to perform and can quickly discharge all pus by negative pressure, especially when there are multi-loculated abscesses, making it very effective in removing pathogens. As PNA does not require the catheter to be left in the body, there is no risk of persistent pain, leakage, or re-infection. Furthermore, the drainage tubes used for PCD require regular sterilization and dressing changes, which can increase medical costs. This suggests that the most appropriate modality of pus removal may depend on the causative pathogen and size of the abscess, and that the modality of pus removal may have clinical implications.

Among our 279 PLA patients, 29 (10.39 %) experienced primary treatment failure, in line with previously reported percentages [4,5,10]. Our multifactorial model showed that alcohol intake, cancer, ICU admission, resolution of fever, and positive blood culture results were positively associated with primary treatment failure. Several other studies of PLA patients also found that a positive blood culture was an independent risk factor for primary treatment failure [11,29]. It is likely that PLA patients with concomitant bloodstream infections have greatly weakened immunity, a condition that can aggravate PLA and possibly lead to invasive liver abscess syndrome, with infections of other organ systems, including meningitis, endophthalmitis, necrotizing fasciitis, and lung abscess [30,31]. The strain of KP responsible for PLA may also affect primary treatment failure [6].

Despite the use of effective treatments, our non-KPPLA group had a poorer prognosis and a higher Charlson comorbidity index, indicting a greater burden from underlying diseases. Tumors were more common the non-KPPLA group, and this may be related to the poor prognosisof this group. In addition, the non-KPPLA group had two AIDS patients, each with a Charlson comorbidity index of 6, and this also contributed to the poorer prognosis of this group. Patients in the non-KPPLA group were infected with a variety of bacterial species, some of which are associated with poor prognosis [23,32]. For example, *Escherichia coli* is believed to be closely related to biliary tract involvement, and these patients can have complex underlying diseases and low immunity due to cancer and malnutrition, which may contribute to their poor prognoses [6,19]. In addition, cytolysins, serine protease, and hyaluronidases, which are related to virulence factors in *Enterococcus*, could affect intracellular killing and phagocytosis of other pathogens, leading to increased dissemination and infection, and possibly contributing to the poor prognosis of the non-KPPLA group [33,34]. Unexpectedly, we also found that alcohol intake was associated with an increased rate of primary treatment failure. Chronic alcohol consumption can affect the structure of the intestinal flora, such decreasing the level of *Bacteroidetes* and increasing the level of *Proteobacteria*, and this may make it difficult for these patients to contain intestinal bacterial infections [35]. Chronic alcohol consumption can also reduce the expression of intestinal mucoprotein 2 and disrupt intestinal tight junction proteins, thereby impairing intestinal barrier function and increasing intestinal permeability [36]. Intestinal dysbiosis and increased intestinal permeability can increase the translocation of pathogen-associated molecular patterns (PAMPs), which are recognized by immune receptors on certain cells (such as hepatic stellate cells and Kupffer cells in the liver) and can then initiate an inflammatory cascade that possibly leads to liver fibrosis [37].

4.1. Limitations

This study has several limitations. The first limitation is that it was a retrospective study performed at a single center, so the results (especially regarding the superiority of PNA over PCD) may not generalizable to other populations, particularly to populations outside Asia. Further confirmation of these findings will require a multicenter study. Second, the relatively small number of patients in the non-KPPLA group and the unequal numbers in the KPPLA and non-KPPLA groups may be a considered a weakness. Another limitation is that patients in the non-KPPLA group were likely infected by different non-KP bacteria, and it may be problematic to classify them all in a single group. Further research with a much larger study population is needed to compare groups of PLA patients that were infected by specific bacteria to address this issue and confirm the conclusions of our study. Furthermore, due to the low mortality rate of KPPLA, it will be difficult to conduct a comprehensive analysis of the impact of different KP subtypes on prognosis. Although this is simply indicative of the predominance of KPPLA in our study population, a larger cohort study is needed to confirm our findings.

5. Conclusion

Our study showed that KP was the predominant pathogen in PLA patients in our study population from Hangzhou. A retrospective analysis showed that the management strategies and prognosis of patients with KPPLA and non-KPPLA abscesses were different, in that the non-KPPLA patients had longer hospital stays and worse prognoses. The PNA and PCD modalities of pus removal achieved satisfactory outcomes, but PNA was associated with a shorter hospital stay and reduced costs, especially in KPPLA patients with abscesses less 10 cm in diameter.

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Ethics statement

This study was reviewed and approved by the Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine (No. 2023-0115).

Data availability statement

Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Qiaomai Xu: Writing – original draft, Formal analysis, Data curation, Conceptualization. **Changhong Liu:** Writing – original draft, Formal analysis. **Zhengjie Wu:** Formal analysis, Data curation. **Shumeng Zhang:** Formal analysis. **Zhuoling Chen:** Data curation. **Yu Shi:** Resources. **Silan Gu:** Writing – review & editing, Resources, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

List of standard abbreviations

PLA	pyogenic liver abscess
KP	*Klebsiella pneumoniae*
KPPLA	*Klebsiella pneumonia* pyogenic liver abscess
non-KPPLA	non-*Klebsiella pneumonia* pyogenic liver abscess
PNA	percutaneous needle aspiration
PCD	pigtail catheter drainage
hvKP	hypervirulent *Klebsiella pneumoniae*
AST	aspartate transaminase
SCr	serum creatinine
ALT	alanine transaminase
CRP	C-reactive protein
ALP	alkaline phosphatase
SDs	standard deviations
IQRs	interquartile ranges
ICU	intensive care unit

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